Split-bolus dual-energy CT urography: protocol optimization and diagnostic performance for the detection of urinary stones

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Abstract: PURPOSE: Prospective protocol optimization, determination of image quality and diagnostic performance of virtual non-enhanced images (VNEI) derived from split-bolus dual-energy computed tomography (DECT) urography in patients with urinary stones. METHODS: IRB-approved, prospective study of 100 patients who, after written informed consent, underwent single-energy, non-enhanced CT and split-bolus, contrast-enhanced DECT (30 + 50 mL of contrast media; combined nephro-urographic acquisition). DECT was performed using setting A (80/140 kVp) in the first 20, and setting B (100/140 kVp) in the second 20 patients. Tin filtration was used in all patients. After a pre-analysis of VNEI quality, 60 additional patients were examined using setting B. Two readers qualitatively and quantitatively determined image quality of all weighted-average DECT images regarding urinary tract opacification (n = 100), and all VNEI regarding quality of iodine subtraction and urinary stone detection (n = 80). True nonenhanced (TNEI) images were the standard of reference for statistical analysis (inter-reader variability and diagnostic performance characteristics). RESULTS: The urinary tract was completely opacified in 94% (94/100) of patients. Iodine subtraction was improved ($p < 0.01$) and image noise of VNEI was lower ($p < 0.05$) in DECT setting B. On VNEI, 83% (86/104) of urinary stones were correctly identified and 17% (18/104) were missed. Stones missed (2.5 mm, 1-4) were significantly smaller than stones correctly identified (5 mm, 2-27; $p < 0.001$). Diagnostic accuracy was 98% on a per-renal-unit basis and 96% on a per-patient basis. Inter-reader agreements were excellent (= 0.91-1.00; ICC = 0.86-0.99). CONCLUSIONS: Split-bolus DECT urography was technically feasible and quality of VNEI was improved with the 100/140 kVp setting. Detection of urinary stones <4 mm on VNEI was limited.

DOI: https://doi.org/10.1007/s00261-013-9992-9

Originally published at:
Karlo, Christoph A; Gnannt, Ralph; Winklehner, Anna; Fischer, Michael A; Donati, Olivio F; Eberli, Daniel; Sulser, Tullio; Alkadhi, Hatem; Stolzmann, Paul (2013). Split-bolus dual-energy CT urography: protocol optimization and diagnostic performance for the detection of urinary stones. Abdominal imaging, 38(5):1136-1143.
DOI: https://doi.org/10.1007/s00261-013-9992-9

Abdominal Imaging

Published online: 17 March 2013
Abdom Imaging (2013) 38:1136–1143
DOI: 10.1007/s00261-013-9992-9

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Abstract

Purpose: Prospective protocol optimization, determination of image quality and diagnostic performance of virtual non-enhanced images (VNEI) derived from split-bolus dual-energy computed tomography (DECT) urography in patients with urinary stones.
Methods: IRB-approved, prospective study of 100 patients who, after written informed consent, underwent single-energy, non-enhanced CT and split-bolus, contrast-enhanced DECT (30 + 50 mL of contrast media; combined nephro-urographic acquisition). DECT was performed using setting A (80/140 kVp) in the first 20, and setting B (100/140 kVp) in the second 20 patients. Tin filtration was used in all patients. After a pre-analysis of VNEI quality, 60 additional patients were examined using setting B. Two readers qualitatively and quantitatively determined image quality of all weighted-average DECT images regarding urinary tract opacification ($n = 100$), and all VNEI regarding quality of iodine subtraction and urinary stone detection ($n = 80$). True nonenhanced (TNEI) images were the standard of reference for statistical analysis (inter-reader variability and diagnostic performance characteristics).
Results: The urinary tract was completely opacified in 94% (94/100) of patients. Iodine subtraction was improved ($p < 0.01$) and image noise of VNEI was lower ($p < 0.05$) in DECT setting B. On VNEI, 83% (86/104) of urinary stones were correctly identified and 17% (18/104) were missed. Stones missed (2.5 mm, 1–4) were significantly smaller than stones correctly identified (5 mm, 2–27; $p < 0.001$). Diagnostic accuracy was 98% on a per-renal-unit basis and 96% on a per-patient basis. Inter-reader agreements were excellent ($\kappa = 0.91$–1.00; ICC = 0.86–0.99).
Conclusions: Split-bolus DECT urography was technically feasible and quality of VNEI was improved with the 100/140 kVp setting. Detection of urinary stones <4 mm on VNEI was limited.

Key words: Multidetector-row computed tomography—Urography—Contrast media urinary lithiasis—Split-bolus protocol

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Computed tomography urography (CTU) is routinely performed to evaluate the urinary tract in patients with hematuria, urinary tract malignancies, and chronic urolithiasis [1, 2]. A standard CTU exam consists of multiple data acquisitions before and after the administration of contrast material and is therefore associated with a considerable radiation exposure to the patient [2]. Today, various techniques are in place to keep the radiation exposure of CTU as low as possible. One such technique is the implementation of a split-bolus contrast injection protocol, which allows for the combined acquisition of two contrast-enhanced CTU phases, most commonly the nephrographic phase and urographic phase [3–8]. Another possibility to reduce radiation exposure is to perform dual-energy computed tomography (DECT), which offers the reconstruction of virtual non-enhanced images (VNEI) by subtracting iodine content from contrast-enhanced DECT data. VNEI, which may be generated from either nephrographic- or urographic-phase DECT data, have the potential to replace true non-enhanced images (TNEI) for selected indications including urinary stone detection [9–12]. Recently, Takeuchi et al. investigated the feasibility of combining a split-bolus

Table 1. Patient demographics and reasons for referral

Total number of patients	100
Female/male	41% (41/100)/59% (59/100)
Median age (range) (years)	47 (18–92)
Median body mass index (range) (kg/m^2)	24.8 (17–35)
Reasons for referral	
Unclear hematuria	86 (86%)
Chronic urolithiasis	14 (14%)

contrast injection protocol and VNEI generated from DECT. However, Takeuchi et al. [13] performed all exams exclusively using a tube voltage setting of 80/140 kVp on a first-generation dual-source CT scanner. Using a second-generation dual-source CT scanner, Mangold et al. investigated the diagnostic accuracy of VNEI generated from urographic-phase DECT for the detection of urinary stones and reported limited accuracy regarding the detection of stones smaller than 3 mm. However, Mangold et al. [9] compared two DECT tube voltage settings (80/140 and 100/140 kVp) and recommended to apply the 100/140 kVp setting because of improved iodine subtraction [9]. Similar to Mangold et al., Takahashi et al. evaluated the detectability of urinary stones on VNEI generated from nephrographic-phase DECT and reported limited detection rates for small urinary stones. However, the study by Takahashi et al. was performed retrospectively and all VNEI were reviewed by two radiologists in consensus, thus lacking inter-reader variability assessment. Moreover, the section thickness of all TNEI, which served as the standard of reference, was 5 mm, as compared to 1.5 mm for all VNEI [10].

Therefore, the objectives of our study were to prospectively compare image quality of VNEI derived from either the 80/140 or 100/140 kVp DECT tube voltage settings in combination with a split-bolus contrast injection protocol and to assess inter-reader agreement as well as diagnostic performance of split-bolus DECT urography for urinary stone detection.

Materials and methods

Patients

The institutional review board approved this prospective study. Each patient provided written informed consent prior to CT. Between April and September 2011, a total of 107 consecutive patients were referred by our institution's urologists to undergo CT urography at our department for unclear hematuria or chronic urolithiasis. Seven patients were excluded from study participation due to renal insufficiency, defined as an estimated glomerular filtration rate lower than 45 mL/min/mm^2 [14]. None of the patients had contraindications for the administration of contrast material, none was pregnant.

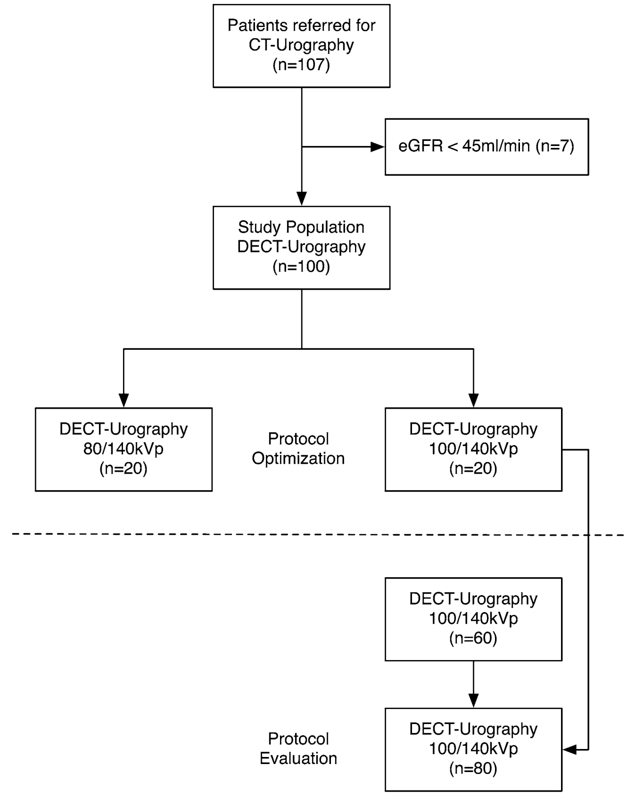

Fig. 1. Flow chart illustrating study design (*eGFR* estimated glomerular filtration rate, *DECT* dual-energy computed tomography).

Finally, 100 patients were enrolled (median age, 47 years; range, 18–92; 59 male) Patient characteristics and reasons for referral are summarized in Table 1.

Data acquisition and reconstruction

All CT examinations were performed using a 128-slice dual-source CT scanner (Definition Flash, Siemens Medical, Forchheim, Germany). Pre-contrast single-energy CT of the entire abdomen and pelvis was performed in all patients prior to the administration of contrast material. Using a dual-head power injector (flow rate, 3.5 mL/s), contrast material (iopromide, Ultravist300, 300 mg/mL, Bayer Schering Pharma, Berlin, Germany) was applied using a split-bolus protocol: First, 30 mL of contrast were injected into an antecubital vein followed by a 40-mL saline bolus. After 540 s, a second bolus of contrast (50 mL) was injected, followed by another 40 mL saline bolus. After another 90 s (total delay after the initiation of the first bolus, 630 s), DECT data was acquired using tube voltage setting A (80/140 kVp) in the first 20 and tube voltage setting B (100/140 kVp) in the second 20 patients. After comparing image quality between VNEI generated from tube voltage settings A and B to optimize the DECT protocol, 60 additional patients were analyzed using the tube voltage setting that

Table 2. Scan parameters

Tube voltage setting	120 kVp	80/140 kVp	100/140 kVp
Tube current time product (mAs/rotation)	100	420/310	210/160
Tin filter	–	Yes	Yes
Slice collimation	128 × 0.6 mm	2 × 64 × 0.6 mm	2 × 64 × 0.6 mm
Gantry rotation time	0.5 s	0.5 s	0.5 s
Pitch	0.7	0.7	0.7
Reconstruction slice thickness	2.0 mm	2.0 mm	2.0 mm
Reconstruction increment	1.6 mm	1.6 mm	1.6 mm
Reconstruction kernel	B30f	D30f	D30f

demonstrated improved iodine subtraction (see Fig. 1 for study design). Tin filtration was used in all patients. Scan and reconstruction parameters are summarized in Table 2. DECT parameters were chosen to result in a similar volume CT dose index ($CTDI_{vol}$) as compared with the standard single-energy CT urography protocol ($CTDI_{vol}$ = 15 mGy) of our institution. All weighted-average, contrast-enhanced DECT images were generated using a composition ratio of 0.5 [9, 10, 15]. All VNEI were reconstructed using semi-automated software (Liver VNC, Dual Energy Syngo, Siemens).

Each patient's body size and weight were noted by the CT technician prior to the exam, and the body mass index (BMI) of each patient was calculated.

Data analysis

Two board-certified radiologists (R.G. and A.W.) independently performed all image analyses. They first analyzed the first 40 patients and after a preliminary analysis to optimize the DECT protocol, they analyzed 60 additional patients. To subjectively determine image quality of VNEI, both readers assessed the quality of iodine subtraction as follows:

- *complete iodine subtraction*, no residual contrast material within the urinary tract;
- *sufficient iodine subtraction*, faint contrast material within the urinary tract;
- *incomplete iodine subtraction*, substantial residual contrast material within the urinary tract.

To determine image noise as a measure of objective image quality, both readers placed a circular region of interest (ROI) in the right liver lobe on the level of the main portal vein in each patient on VNEI and TNEI and noted the standard deviation of the attenuation in Hounsfield Units (HU). Care was taken to exclude liver vasculature and bile ducts from the ROI.

To subjectively determine image quality of weighted-average images regarding the opacification of the urinary tract, both readers assessed for the presence or absence of contrast material within the pelvicaliceal system, ureter, and bladder in all patients.

Both readers independently assessed all VNEI and, after a time interval of 4 weeks to minimize recall bias, all TNEI in a randomized order for the presence or absence of urinary stones and measured the longest diameter (in mm) and attenuation (in Hounsfield Units, HU) of each urinary stone on VNEI and TNEI using fixed window/level settings (500/2000 HU). In addition, each reader noted the location of the urinary stone on both VNEI and TNEI (i.e., pelvicaliceal system, ureter, bladder; left or right). Discrepant cases were re-evaluated by both readers to achieve consensus.

Statistical analysis

Continuous variables were described as mean ± standard deviation if normally distributed and as medians if non-normally distributed. Categorical variables were expressed as frequencies and percentages. All statistical analyses were performed using commercially available software (SPSS 19, IBM, Armonk, NY, USA). *P* values <0.05 were considered to yield statistical significance.

To determine inter-reader agreement for the assessment of categorical variables, Cohen's Kappa (κ) was calculated. To determine inter-reader agreement for the assessment of continuous variables, intraclass correlation coefficient for absolute agreement (ICC) was calculated.

Table 3. Summary of quantitative image analyses and inter-reader agreements

	Reader 1	Reader 2	ICC
Image noise (HU)			
TNEI	21 (14 to 65)	22 (13 to 56)	0.96
VNEI	10 (5 to 66)	11 (5 to 65)	0.86
Pelvicaliceal system (HU)			
TNEI	7 (−11 to 22)	8 (−10 to 21)	0.95
VNEI	11 (−22 to 392)	10 (−17 to 335)	0.99
Renal parenchyma (HU)			
TNEI	30 (24 to 40)	29 (22 to 53)	0.84
VNEI	33 (9 to 45)	33 (10 to 47)	0.91
Bladder (HU)			
TNEI	10 (−5 to 55)	11 (−5 to 51)	0.96
VNEI	6 (−37 to 39)	5 (−15 to 30)	0.80
Urinary stone diameter (mm)			
TNEI	6 (2 to 27)	6 (2 to 27)	0.99
VNEI	5 (2 to 27)	5 (1 to 28)	0.99
Urinary stone attenuation (mm)			
TNEI	636 (143 to 1380)	601 (166 to 1512)	0.92
VNEI	330 (49 to 908)	346 (64 to 909)	0.93

All variables presented as medians; ranges in parentheses
ICC Intraclass Correlation Coefficient for absolute agreement, *TNEI* true nonenhanced images, *VNEI* virtual nonenhanced images

The Wilcoxon rank-sum test was used for assessing differences in the quality of iodine subtraction between tube voltage settings A and B. To assess for differences in patients' age, BMI, attenuation measurements (i.e., renal parenchyma, pelvicaliceal system, and bladder), scan length and dose-length product (DLP) between tube voltage settings A and B, the *t* test for independent samples was used. To assess for differences in gender distribution between tube voltage settings A and B, Mann–Whitney *U* test was used. To assess for differences in image noise between VNEI and TNEI, the *t* test for paired samples was used.

To assess for differences in urinary stone diameters and attenuation between VNEI and TNEI, the *t* test for paired samples was used. To assess for differences in mean urinary stone diameter between urinary stones missed and urinary stones correctly identified on VNEI, the *t* test for independent samples was used. Regarding the detection of urinary stones, diagnostic accuracy, sensitivity, and specificity were derived from Chi square tests of contingency, 95% confidence intervals (CI) were calculated on a per-stone, per-renal unit (defined as the pelvicaliceal system and ureter of one kidney), and per-patient basis (defined as the presence or absence of at least one urinary stone in a single patient). TNEI images served as the standard of reference.

Results

Inter-reader agreements

Inter-reader agreements regarding the assessment of urinary tract opacification on weighted-average images ($\kappa = 1.00$) and the assessment of iodine subtraction on VNEI ($\kappa = 0.91$) were excellent. Inter-reader agreements regarding the measurement of all continuous variables were excellent (Table 3). Therefore, the mean of both readers' measurements was used for further analyses.

Table 4. Comparison between tube voltage settings A and B (protocol optimization)

	Protocol A	Protocol B	*p* value
Tube voltage setting	80/140 kVp	100/140 kVp	–
Number of patients	20	20	–
Gender (male/female)	13/7	11/9	0.600
Body mass index (kg/m^2)	28 (18 to 35)	24 (17 to 33)	0.120
Image noise (HU)[a]	18 (4 to 57)	12 (−15 to 24)	0.014
Pelvicaliceal system (HU)[a]	16 (7 to 193)	2 (−92 to 24)	0.048
Renal parenchyma (HU)[a]	6 (0 to 24)	1 (−16 to 16)	0.004
Bladder (HU)[a]	3 (103 to 25)	7 (−8 to 30)	0.030
Complete iodine subtraction	35% (7/20)	70% (14/20)	<0.001
Sufficient iodine subtraction	30% (6/20)	30% (6/20)	<0.001
Incomplete iodine subtraction	35% (7/20)	–	<0.001

[a]Differences between true (TNEI) and virtual (VNEI) nonenhanced images

Fig. 2. A Transverse contrast-enhanced weighted-average dual-energy CT, true nonenhanced (TNEI) single-energy CT (**B**), and virtual nonenhanced (VNEI) dual-energy CT (**C**) images in a 70-year-old woman with unclear hematuria examined by tube voltage setting B (100/140 kVp). Note the complete subtraction of iodinated contrast material from the bladder between the weighted-average image and the VNEI.

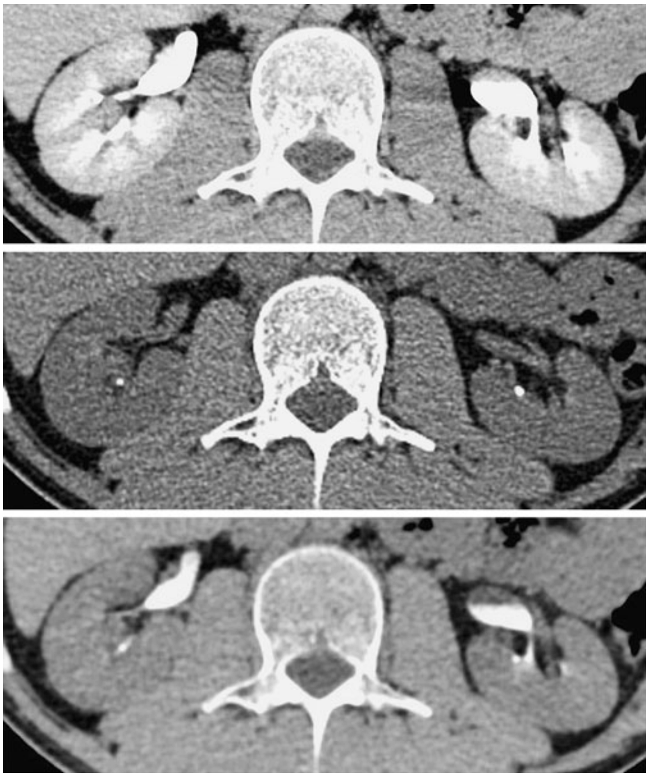

Fig. 3. **A** Transverse contrast-enhanced weighted-average dual-energy CT, true nonenhanced (TNEI) single-energy CT (**B**), and virtual nonenhanced (VNEI) dual-energy CT (**C**) images in a 35-year-old man with chronic urolithiasis examined by tube voltage setting A (80/140 kVp). Note the substantial amount of residual contrast material within the pelvicaliceal system on the VNEI (**C**) when compared to the TNEI (**B**). The bilateral urinary stones, as depicted by the TNEI (**B**), are masked by residual contrast material on the VNEI (**C**) and were thus missed during analysis.

Fig. 4. **A** Transverse contrast-enhanced weighted-average dual-energy CT, true nonenhanced (TNEI) single-energy CT (**B**), and virtual nonenhanced (VNEI) dual-energy CT (**C**) images in a 70-year-old woman with a long history of complicated urolithiasis examined using tube voltage setting B (100/140 kVp). The VNEI (**C**) allows for accurate detection of the left-sided urinary stone.

Optimization of DECT protocol

Patient characteristics were similar between tube voltage settings A and B. Quality of iodine subtraction on VNEI was improved in tube voltage setting B (100/140 kV) when compared to setting A (80/140 kV).

Differences in attenuation of the pelvicaliceal system, renal parenchyma, and bladder between TNEI and VNEI were significantly lower for tube voltage setting B (100/140 kV). Therefore, based on the significantly improved iodine subtraction, 60 additional patients were examined using tube voltage setting B (100/140 kV). Results from protocol optimization are summarized in Table 4.

Opacification of the urinary tract

Complete opacification of both pelvicaliceal systems, both ureters, and the bladder was achieved in 94% (94/100) of patients. In 6% (6/100) of patients, contrast material was absent in either both ureters and the bladder ($n = 2$) or in one ureter ($n = 4$) due to distal ureteral obstructions and therefore delayed excretion of contrast material.

Evaluation of DECT protocol

The quality of iodine subtraction on VNEI was evaluated using patients examined by tube voltage setting B ($n = 80$). Complete iodine subtraction was achieved in 63% (50/80) of patients, faint contrast material was found within the urinary tract or renal parenchyma in 31% (25/80), and substantial residual contrast material was detected in 6% (5/80) of patients (Figs. 2, 3).

Attenuation of the renal parenchyma was similar between VNEI and TNEI ($p = 0.38$). In the pelvicaliceal system, there was a non-significant trend towards higher attenuation on VNEI as compared to TNEI ($p = 0.05$). Attenuation of the bladder was significantly lower (difference, 6 ± 10 HU) on VNEI than on TNEI ($p < 0.01$). Image noise was significantly lower (difference, 13 ± 13 HU) on VNEI than on TNEI ($p < 0.001$, Table 2).

Urinary stones

Re-evaluation of images from 4 patients was necessary to resolve discrepancy among readers. Both readers detected 104 urinary stones in 41% (33/80) of patients on TNEI (left pelvicaliceal system, 42.3% [44/104]; right pelvicaliceal system, 45.2% [47/104]; left ureter, 3.8% [4/104]; right ureter, 4.9% [5/104]; bladder, 3.8% [4/104]), and 86 stones in 38% (30/80) of patients on VNEI (left pelvicaliceal system, 46.5% [40/86]; right pelvicaliceal system, 43.0% [37/86]; left ureter, 2.3% [2/86]; right ureter, 4.7% [4/86]; and bladder, 3.5% [3/86]).

On VNEI, 17% (18/104) of stones were missed in 9% (7/80) of patients, because they were either accidentally subtracted together with iodine (89% [16/18]) or masked by residual contrast material, which had not been subtracted completely during VNEI reconstruction (11% [2/18]). Stones missed on VNEI were located in the left pelvicaliceal system (22.2% [4/18]), right pelvicaliceal system (55.6% [10/18]), left ureter (11.1% [2/18]), right ureter (5.5% [1/18]), and bladder (5.5% [1/18]).

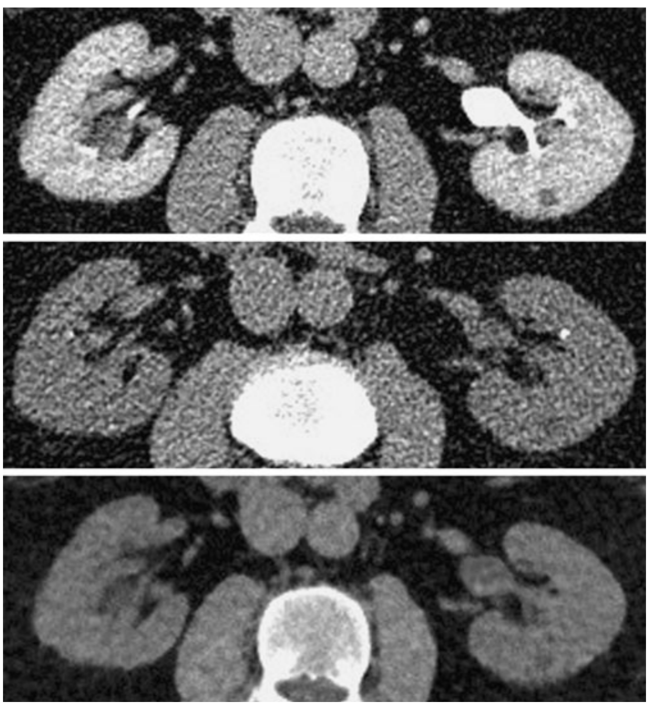

Fig. 5. A Transverse contrast-enhanced weighted-average dual-energy CT, true nonenhanced (TNEI) single-energy CT (**B**), and virtual nonenhanced (VNEI) dual-energy CT (**C**) images in a 57-year-old man with unclear hematuria examined using tube voltage setting B (100/140 kVp). The VNEI fails to depict the left-sided urinary stone due to inadvertent subtraction together with the iodinated contrast material.

Maximum stone diameter was significantly smaller on VNEI (median, 5 mm; range, 2–27 mm) than on TNEI (6 mm, 2–27 mm; $p < 0.005$). Stone attenuation was significantly lower on VNEI (337 HU, 56–909 HU) than on TNEI (619 HU, 154–1446 HU; $p < 0.001$). Stones missed on VNEI (2.5 mm, 1–4 mm) were significantly smaller than stones correctly identified on VNEI (5 mm, 2–27 mm; $p < 0.001$; Figs. 4, 5).

Diagnostic performance characteristics for the detection of stones are summarized in Table 5. No significant differences were found regarding the accuracy of stone detection ($p = 0.82$) between tube voltage settings A and B.

Other imaging findings

A total of 66 renal cysts were detected in 45% (36/80) of patients. 6% (4/66) of renal cysts were complex cysts with contrast enhancement. One patient had a urothelial carcinoma of the renal pelvis with metastases along the ureter and in the bladder; and one patient had an adrenal carcinoma. Information regarding tumor entity was retrieved from histopathology at the end of the study period. Two patients had previously undergone unilateral nephrectomy. Due to the small sample size of lesions other than urinary stones, potential differences in contrast enhancement calculated from either VNEI or TNEI were not investigated in this study.

Radiation dose

By omitting the pre-contrast single-energy CT acquisition, the DLP and the CT dose index could have been reduced by an average of 28% ± 6% (9–51%), from 1003 ± 287 (388–1809) to 716 ± 194 (189–1186) and from 21.4 ± 5.2 (9.2–36) to 15.3 ± 3.5 (4.5–25.1), respectively.

Table 5. Diagnostic performance characteristics for the detection of urinary stones

	Per-stone based analysis	Per-renal unit based analysis	Per-patient based analysis
Diagnostic accuracy	83% (74–89%)	98% (95–100%)	96% (89–99%)
Sensitivity	83% (74–89%)	94% (83–99%)	91% (76–98%)
Specificity	n/a	100% (97–100%)	100% (92–100%)
True positive	86	45	30
True negative	0	112	47
False positive	0	0	0
False negative	18	3	3

95% Confidence intervals in parentheses

Discussion

This study aimed at investigating the feasibility of split-bolus DECT urography and the diagnostic performance in regard to the detection of urinary stones. The study yielded the following results:

First, the split-bolus protocol was technically feasible, as opacification of the complete urinary tract was achieved in 94% (94/100) of patients. Second, the subtraction of iodine during the reconstruction process of VNEI was improved when the DECT data was acquired using tube voltage setting B (100/140 kVp), as visual assessment of VNEI revealed no substantial amount of residual contrast material within the urinary tract in 94% (75/80) of patients. Third, image quality of VNEI was improved and image noise was significantly lower when the DECT data was acquired using tube voltage setting B (100/140 kVp), as differences in attenuation of the pelvicaliceal system, renal parenchyma, and bladder between TNEI and VNEI were significantly lower when compared to tube voltage setting A. Fourth, while 83% (86/104) of urinary stones were correctly identified on VNEI, 17% (18/104) of urinary stones were missed on VNEI because they were either masked by residual contrast material or unintentionally subtracted during the reconstruction process of VNEI. Urinary stones missed on VNEI were significantly smaller than stones correctly identified on VNEI. Finally, the diagnostic accuracy of urinary stone detection on VNEI was 98% (95% CI: 95–100%) on a per-renal unit basis and 96% (95% CI: 89–99%) on a per-patient basis.

Previous studies investigating split-bolus contrast injection protocols for CT urography used total amounts of contrast media of 120 mL [3, 8], 130 mL [7], 145 mL [5], or 175 mL [4]. Our study indicated that a split-bolus contrast injection protocol with a total amount of 80 mL was sufficient in the majority (94%) of patients. However, the concentration of iodine within the urinary tract may increase with an increasing amount of contrast material applied and thus the reconstruction of VNEI may become more challenging at higher doses of contrast material, as previously suggested [9].

Prior to performing the main analyses, we optimized the split-bolus DECT protocol in regard to the quality of iodine subtraction on VNEI. Similar to a recently published report by Mangold et al. [9], we found the quality of iodine subtraction superior when using the 100/140 kVp instead of the 80/140 kVp tube voltage setting. Although iodine subtraction is known to be challenging in DECT imaging, we were able to achieve sufficient iodine subtraction in the majority of our patients. However, as a substantial amount of residual contrast material was present within the urinary tract in 6% (5/80) of patients based on visual analysis, the attenuation of the pelvicaliceal system was slightly (but not significantly) higher on VNEI than on TNEI.

The problem of inadvertent stone subtraction in DECT was addressed by previous studies not applying split-bolus protocols and was attributed to the high attenuation of contrast material in the pelvicaliceal system in combination with small and low-attenuating stones that may be erased from images, especially at higher image noise levels [9–12]. Similarly, the issue of missed urinary stones on VNEI being smaller than those correctly identified was previously reported by Takahashi et al. [10], who found a sensitivity of 64% for the detection of stones smaller than 4 mm. In our study, the median size of urinary stones missed on VNEI was 2.5 mm (range, 1–4 mm). When compared to TNEI, diameter measurements of urinary stones were significantly smaller on VNEI, a finding that was previously reported in other studies as well [10, 12]. Thus, we found the detection of small urinary stones to be limited on VNEI. However, the diagnostic accuracy of urinary stone detection on VNEI reconstructed from split-bolus DECT urography in our study was 98% on a per-renal unit basis and 96% on a per-patient basis, despite of the issues mentioned above.

Split-bolus DECT urography has the potential to contribute to reducing the radiation burden of CT urography. We were able to combine the nephrographic and urographic phases into one combined acquisition using a split-bolus contrast injection protocol. In addition, we were able to reconstruct VNEI from DECT, which resembled TNEI in the majority of patients. Thus, a conventional, three-phasic CT urography protocol might be reduced to just one DECT acquisition. In a recently published study, Takeuchi et al. [13] reported that the reconstruction of VNEI from split-bolus DECT urography was feasible but that—for selected indications—an additional single-energy, non-enhanced CT scan might be necessary in patients with hematuria or urinary tract neoplasms. However, Takeuchi et al. exclusively applied the 80/140 kVp tube voltage setting in a small group of patients ($n = 30$), whereas we used the improved 100/140 kVp tube voltage setting in a larger group of patients ($n = 80$) and were able to achieve improved iodine subtraction. Therefore, when performing split-bolus DECT urography, the 100/140 kVp setting should be used.

We acknowledge the following study limitations: First, we evaluated all patients using DECT and were therefore not able to directly compare radiation dose estimates between split-bolus DECT urography and split-bolus single-energy CT urography. However, by omitting the nonenhanced, single-energy CT acquisition, an average radiation reduction of 28%, ranging from 9% to as high as 51% would have been achieved. Second, the standard of reference for the assessment of urinary stones was not independent from the experimental approach, as the same radiologists evaluated all TNEI and VNEI. However, we implemented a 4-week time interval between the assessment of VNEI and TNEI in order to minimize potential recall bias. Third, we did not assess the performance of the proposed approach in the diagnostic work-up of focal, contrast-enhancing lesions of the kidney or urinary tract due to a relatively small sample size of only four lesions. Finally, the study was carried-out using only the CT machine and software from one specific vendor and thus results may not apply to other vendors in a similar manner.

In conclusion—while the combination of a split-bolus contrast injection protocol and reconstruction of VNEI from DECT urography was feasible in 94% of patients and improved when applying the 100/140 kVp tube voltage setting—a considerable number of urinary stones smaller than 4 mm were missed on VNEI, thus limiting its use as a standard tool in clinical routine.

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